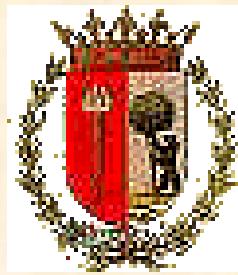


Taller 5. Función endotelial:

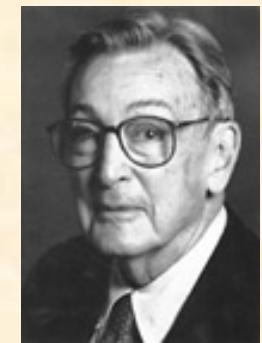
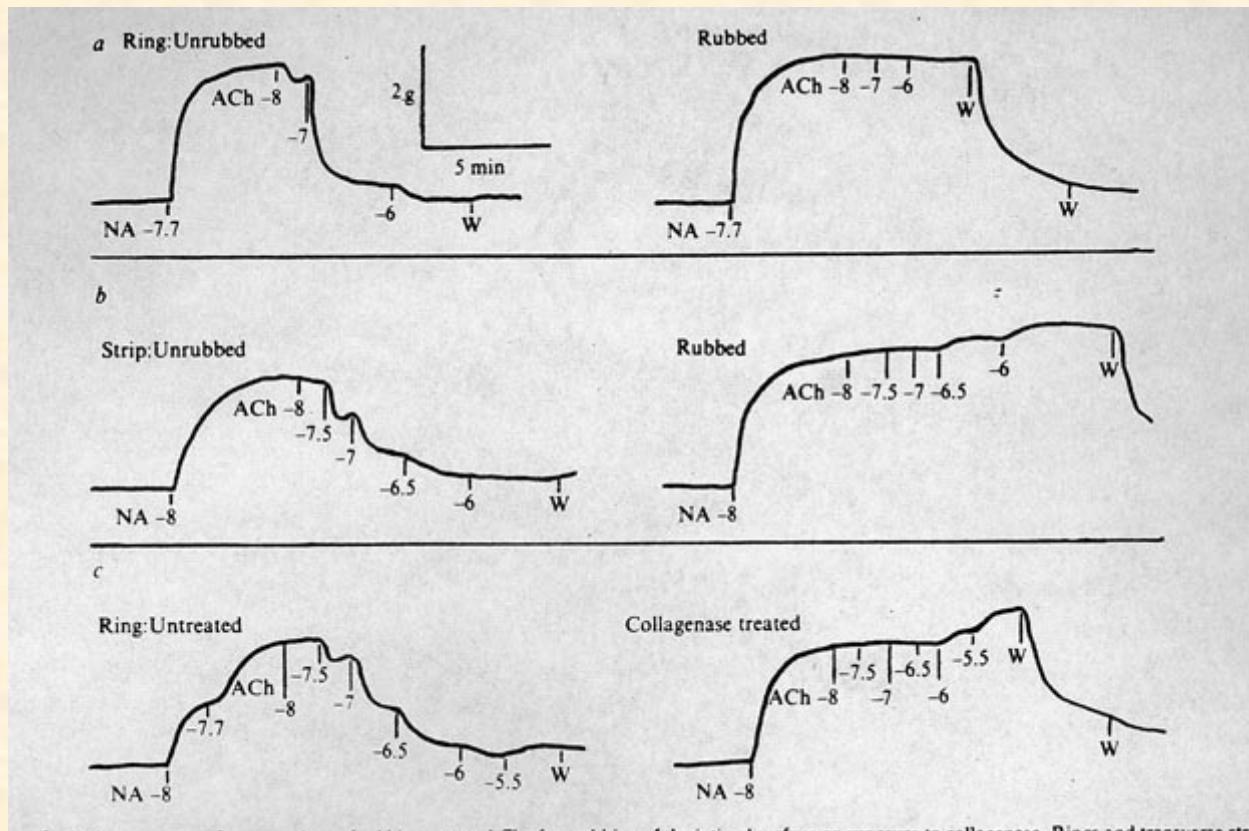
Dr. Jorge F Gómez Cerezo. Servicio de Medicina Interna. Hospital Infanta Sofía

1. El concepto de disfunción endotelial se refiere a:

- 1. Una menor producción de óxido nítrico por el endotelio**
- 2. Una disminución de la vasodilatación dependiente de endotelio.**
- 3. Una menor respuesta a cualquier tipo de vasodilatador.**
- 4. Un aumento de las resistencias vasculares periféricas.**



LIBERACION DE FACTORES VASOACTIVOS DEL ENDOTELIO VASCULAR: FUNCION ENDOTELIAL



R. Furchtgott
Premio Nobel de
Medicina 1998

Furchtgott and Zawadzki; Nature 288: 373-376, 1980

DISFUNCION ENDOTELIAL

Dilataciones dependientes de endotelio

PGI_2

EDHF

NO

producción
inactivación

Contracciones dependientes de endotelio

$\text{TXA}_2/\text{PGH}_2$

ET-1

O^-_2

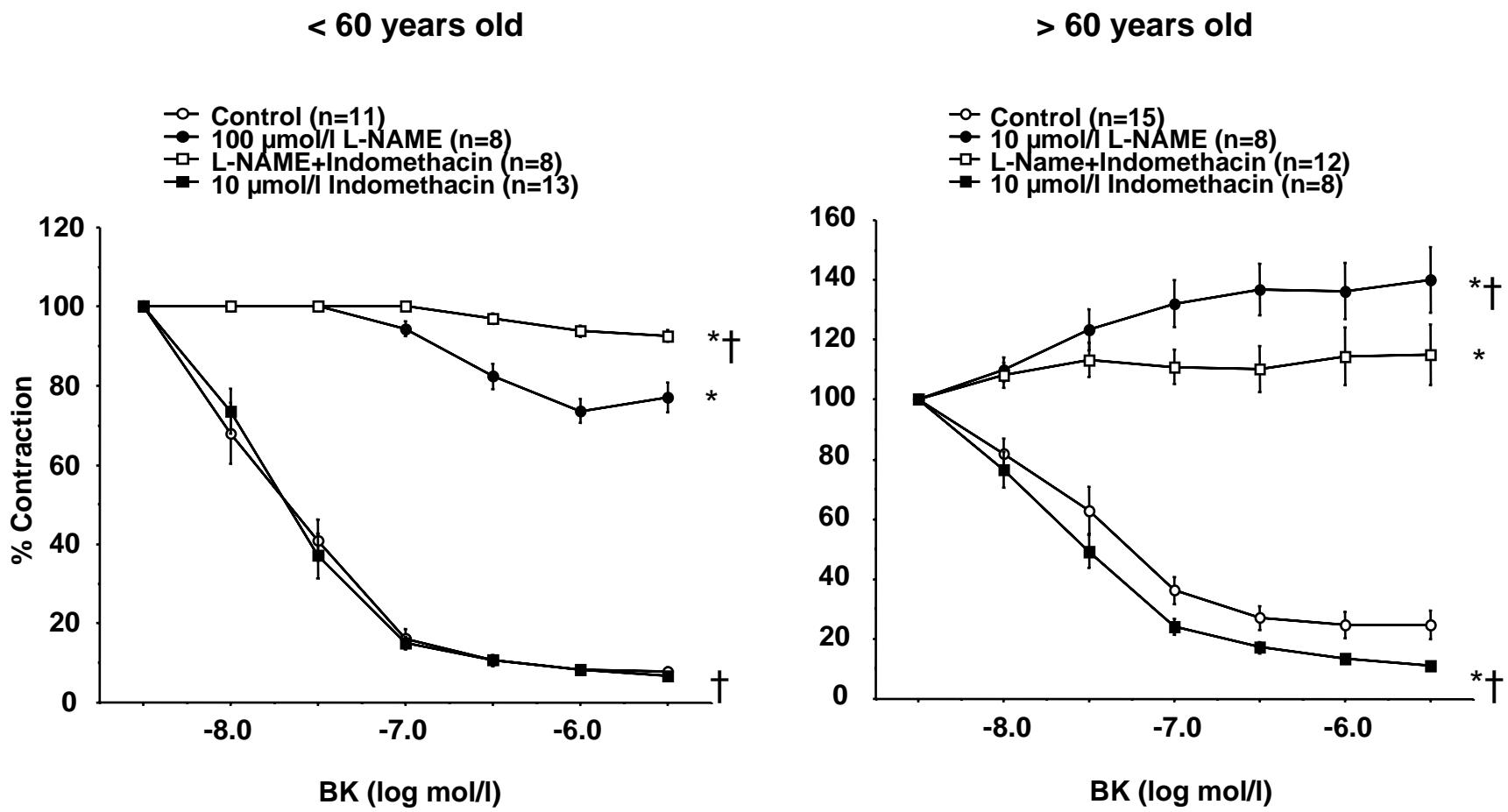


Figure 2

Inflammation
Vasoconstriction
Platelet aggregation
Procoagulant
Proliferative

Disease

- Ang II
- Endothelin
- Free radicals
- TxA₂

Health

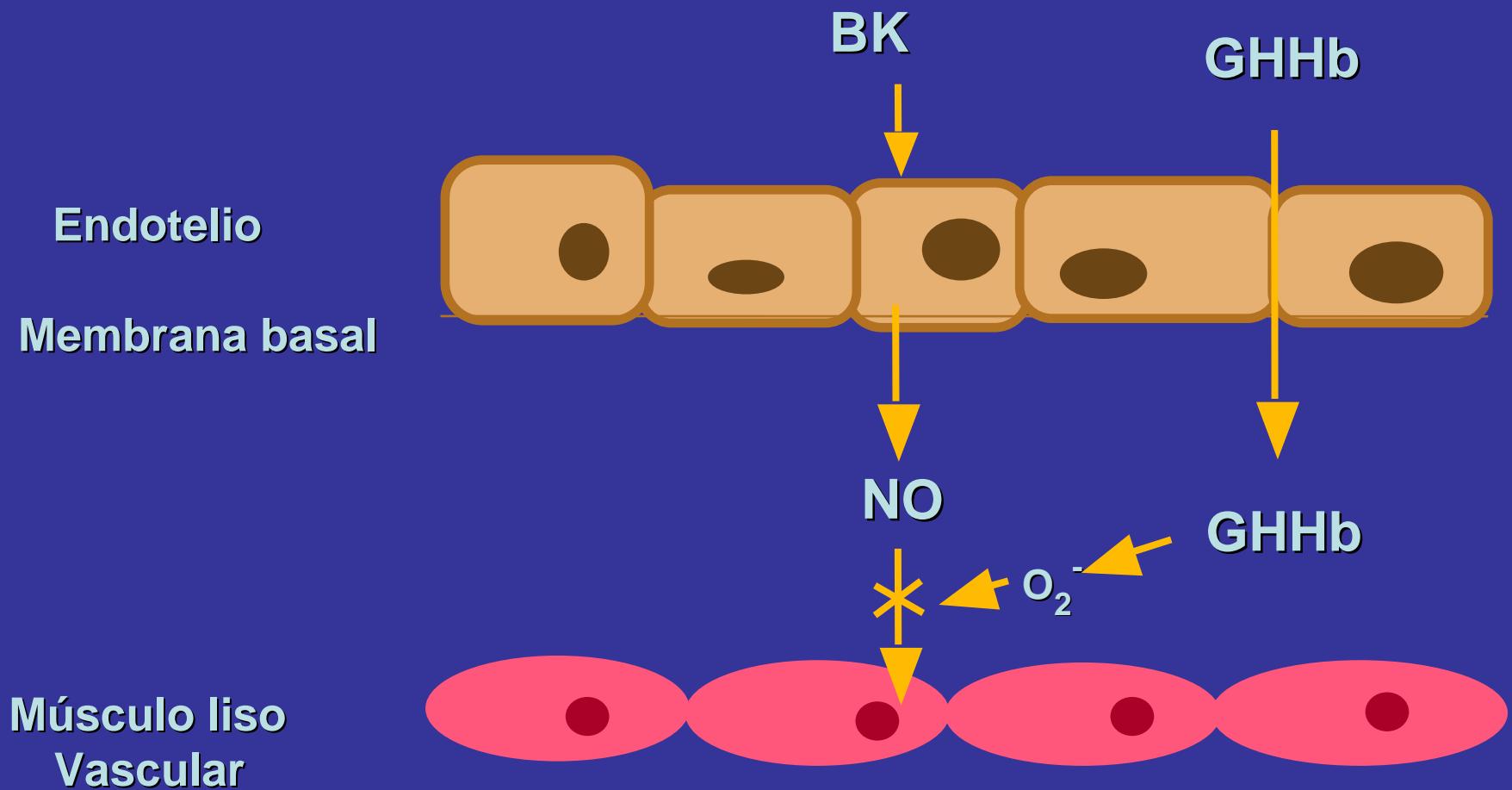
- Nitric Oxide
- PGI₂
- EDHF

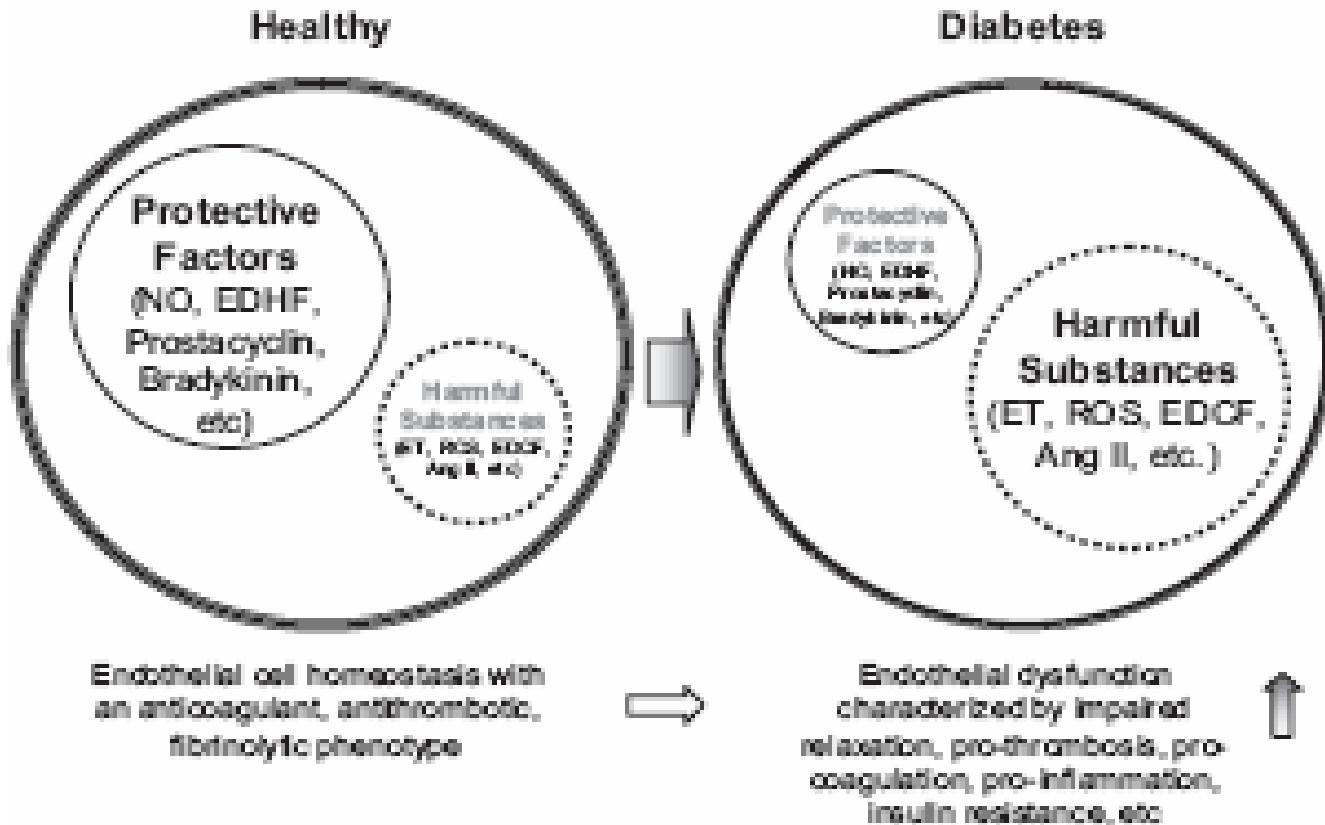
Antiplatelet
Vasodilation
Antiinflammatory
Antiproliferative
Fibrinolysis

Rodríguez-Mañas et al. Circulation 88: 2111-2116, 1993

Angulo et al. Hypertension 28: 583-592, 1996

Vallejo et al. Diabetologia 43: 83-90, 2000





Taller 3. Función endotelial:

¿Cómo medirla?

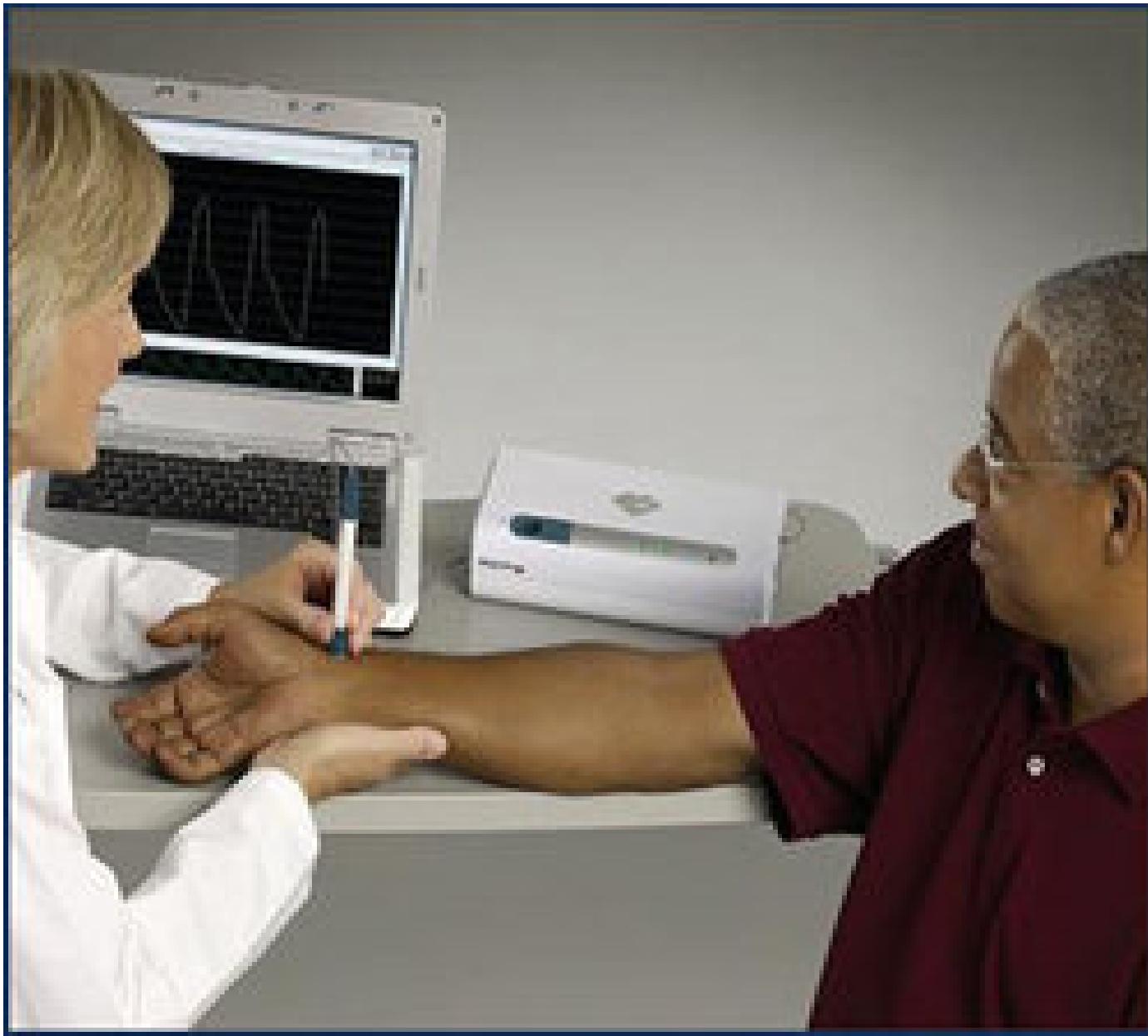
Summary of modalities for assessing endothelial function

Microvasculature

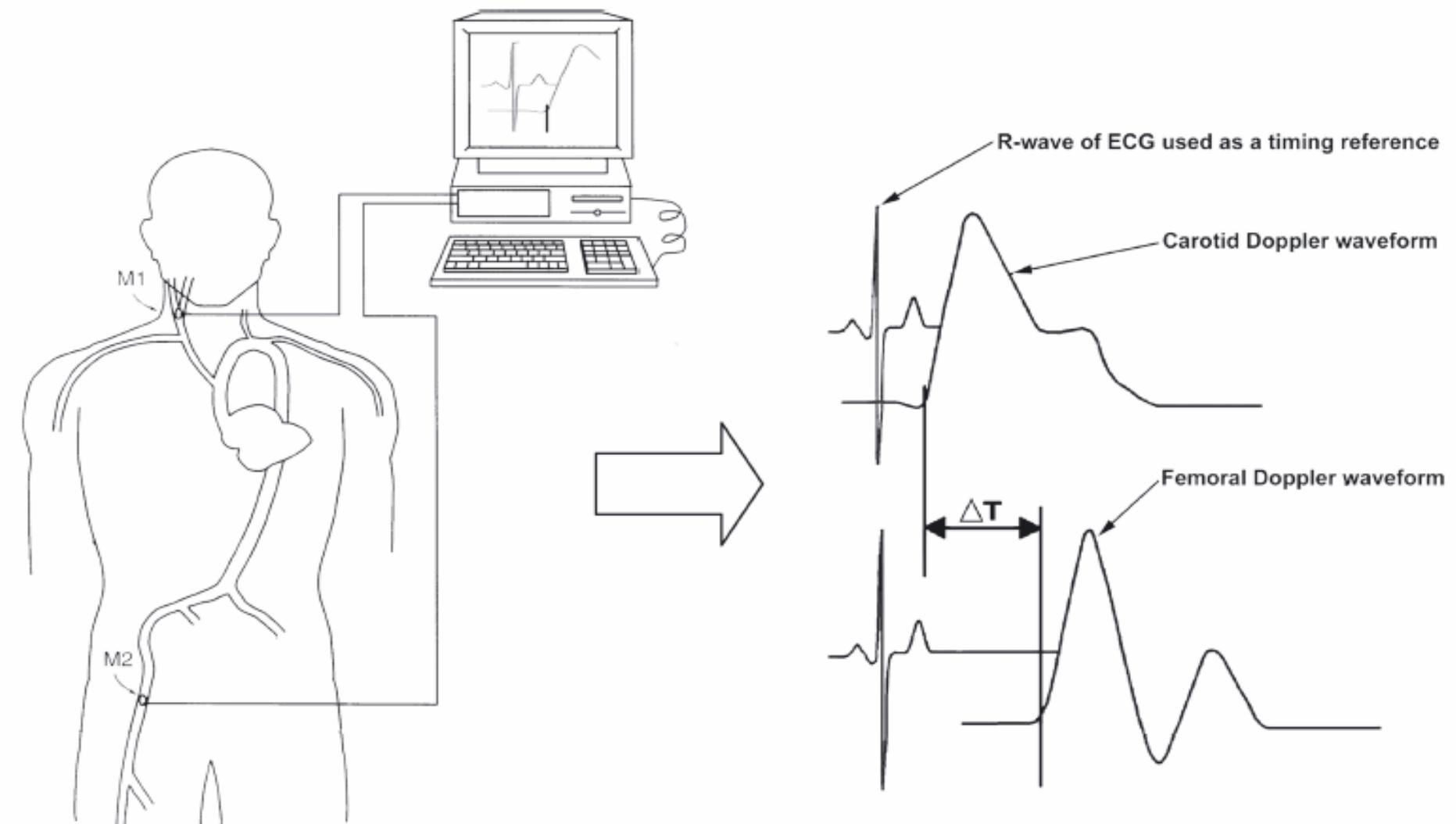
1. Pulse arterial tonometry
2. Coronary blood flow – Doppler
3. Coronary blood flow – positron emission tomography
4. Forearm impedance plethysmography
5. Pulse wave analysis (applanation tonometry)
6. Cardiac magnetic resonance
7. Laser Doppler flowmetry of the skin
8. Hyperemic velocity post occlusion

Conduit vessel

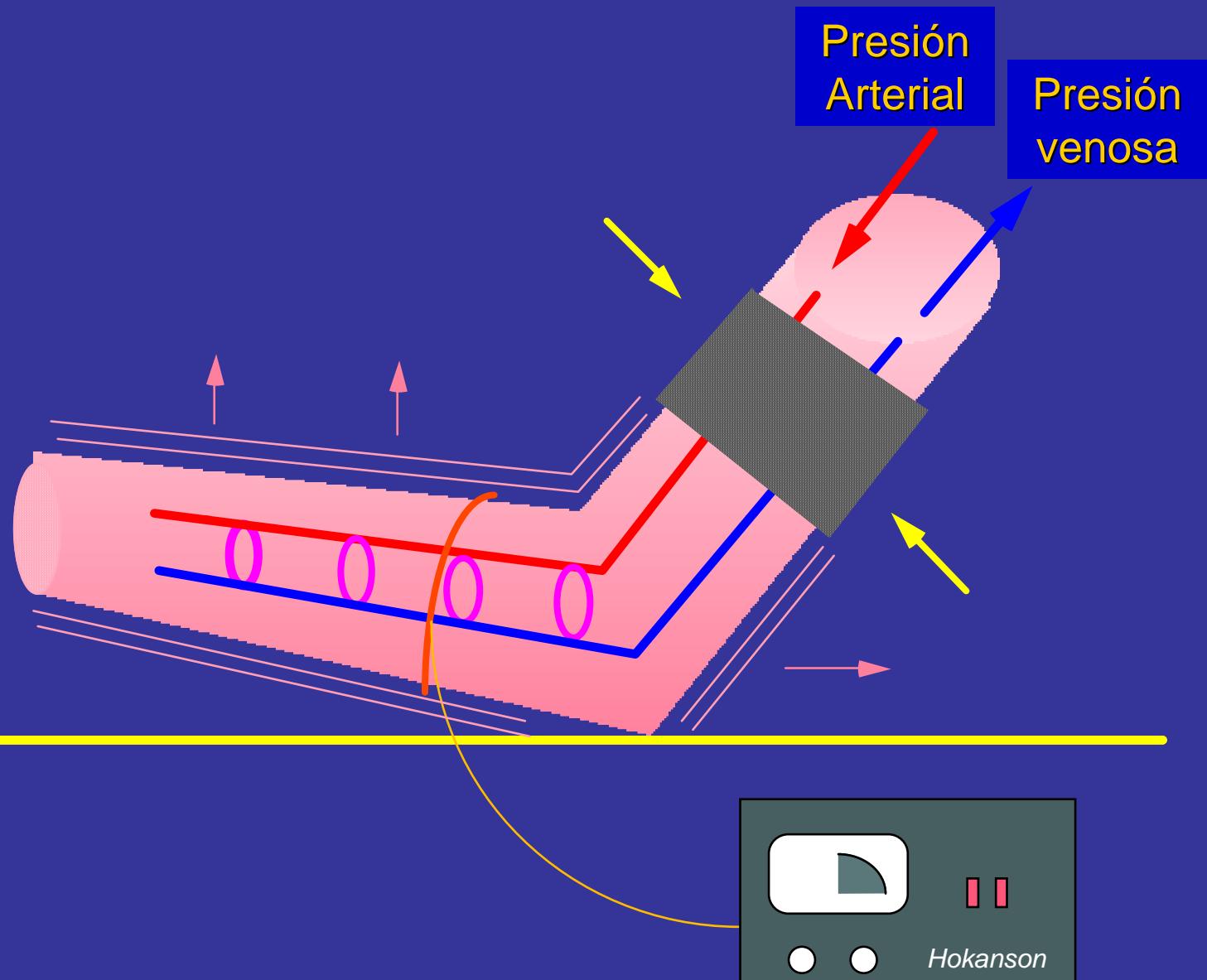
1. Flow-mediated dilation
2. Quantitative coronary angiography
3. Flow-mediated constriction



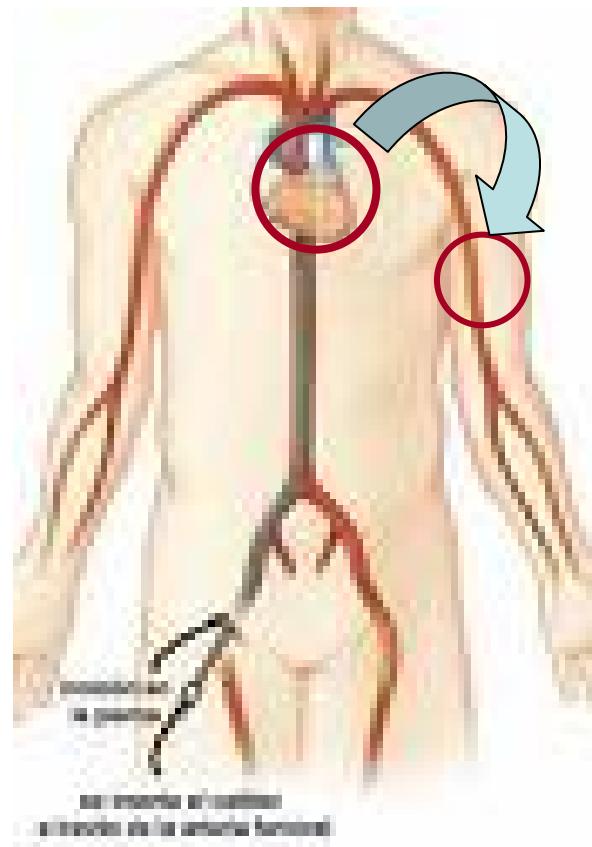
VELOCIDAD DE LA ONDA DE PULSO

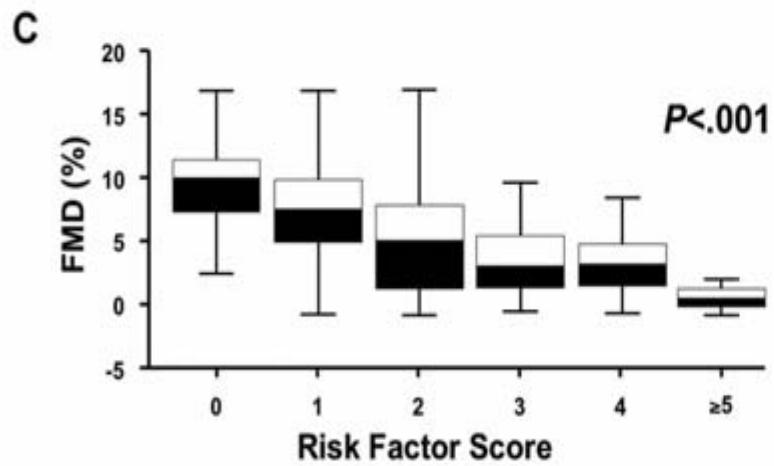
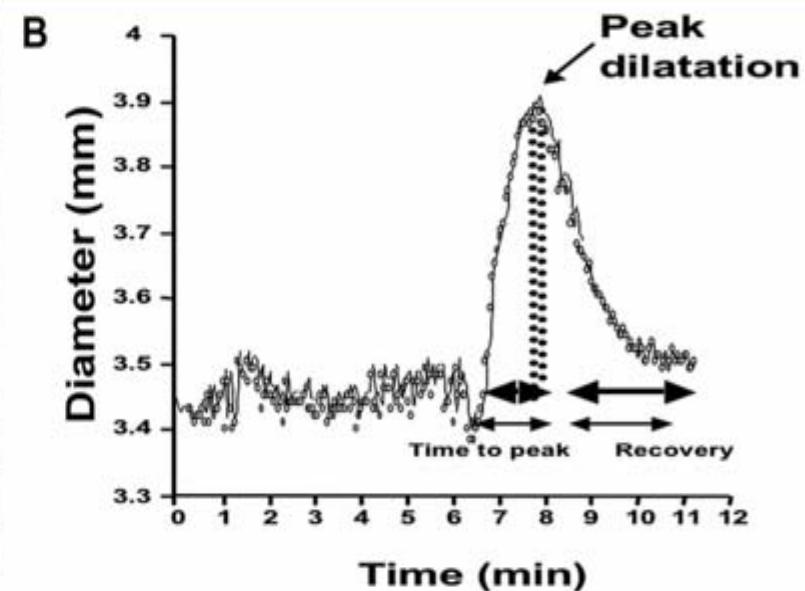
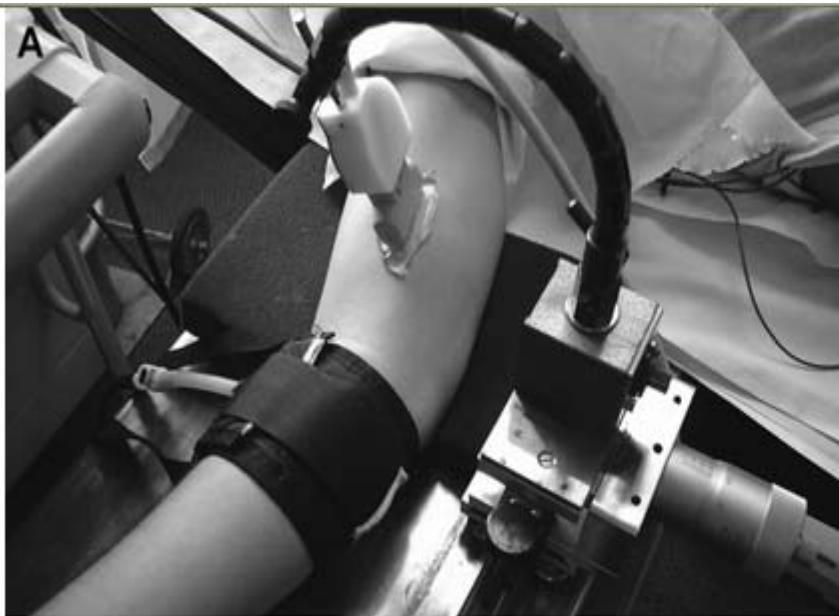




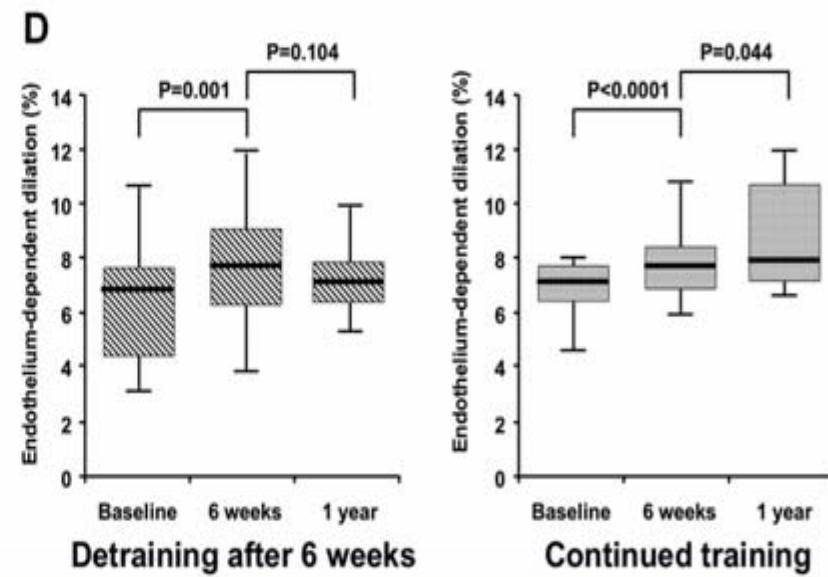


DISFUCIÓN CORONARIA/BRAQUIAL





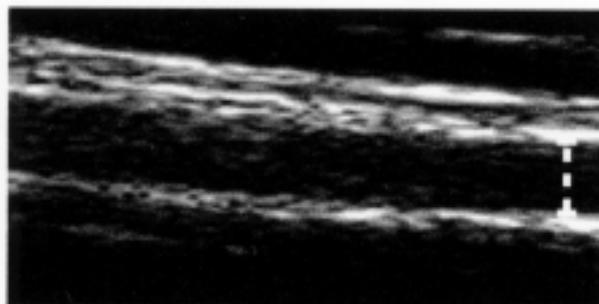
Cholesterol, smoking, mean blood pressure,
family history, age, gender.



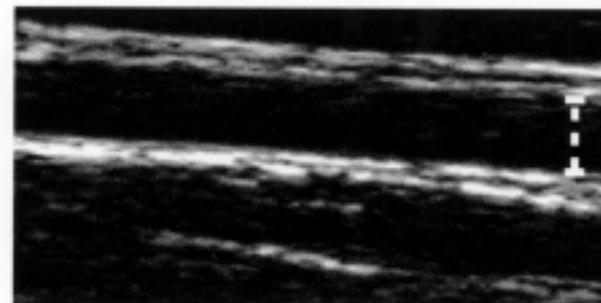
Arteria braquial

A

basal



1 minuto

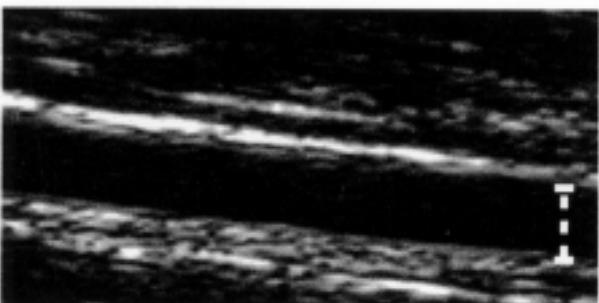


2.5 mm

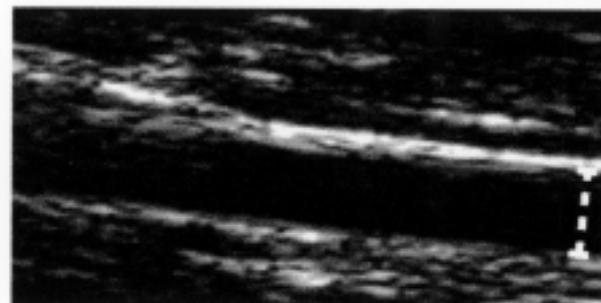
2.6 mm

B

basal



1 minuto

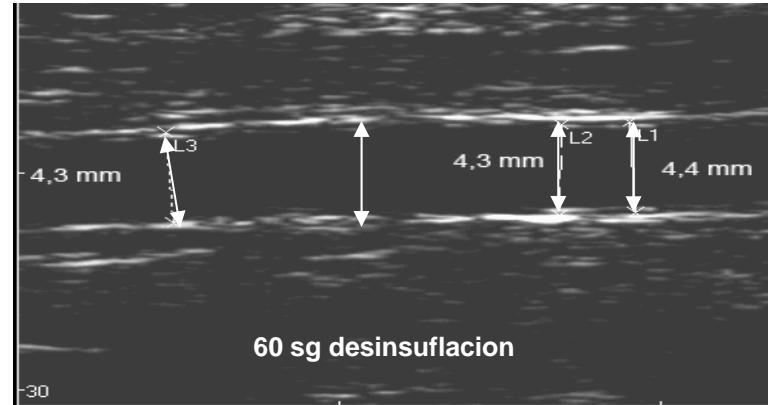
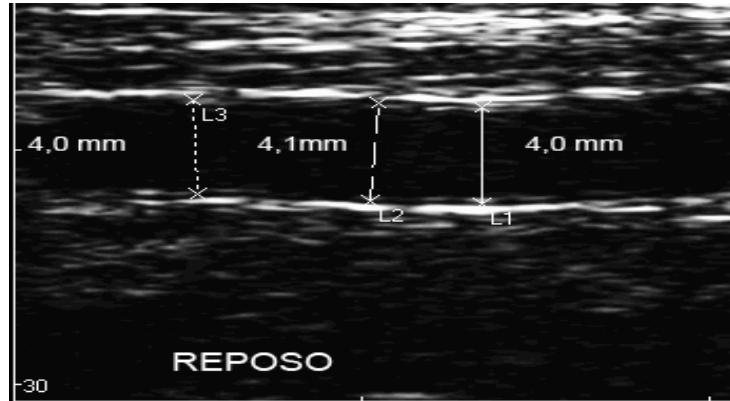


2.5 mm

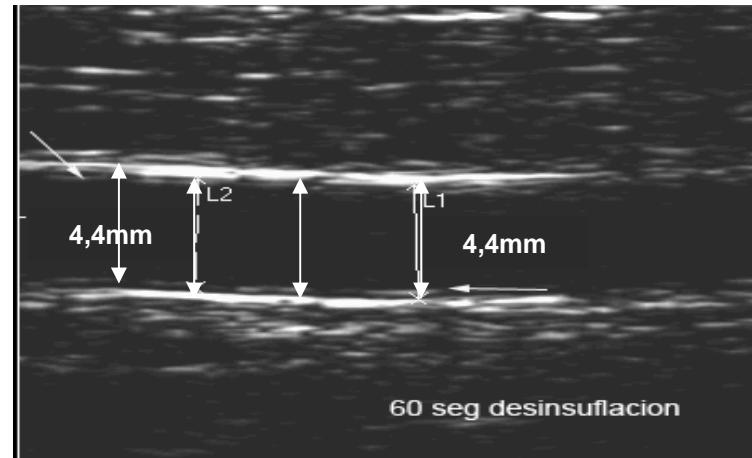
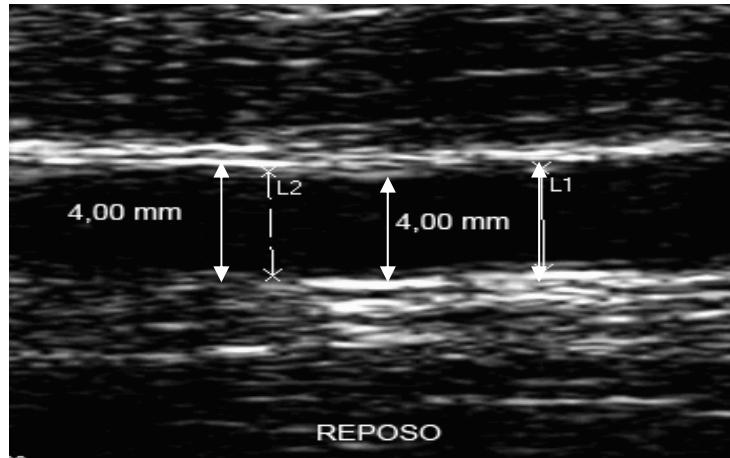
2.8 mm

Función endotelial: protocolo

Basal



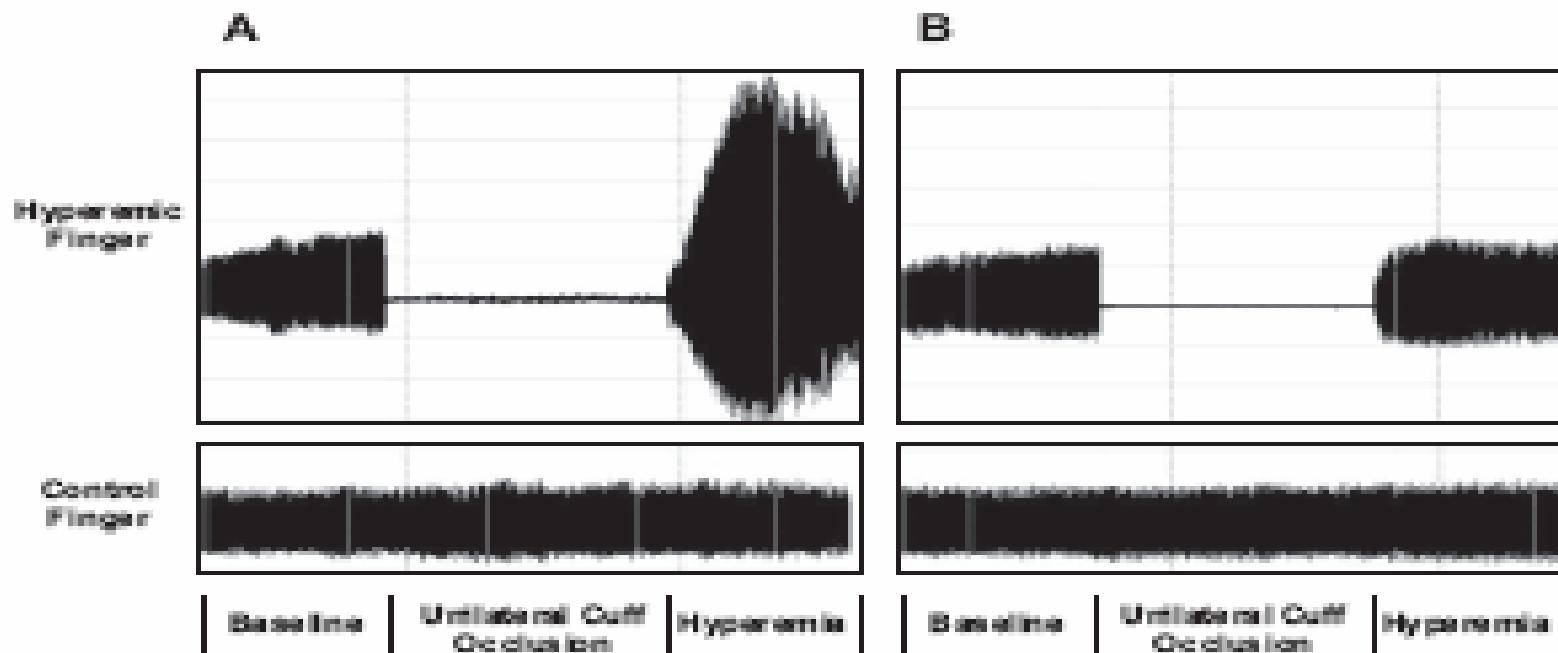
Dos semanas



ENDO- PAT 2000





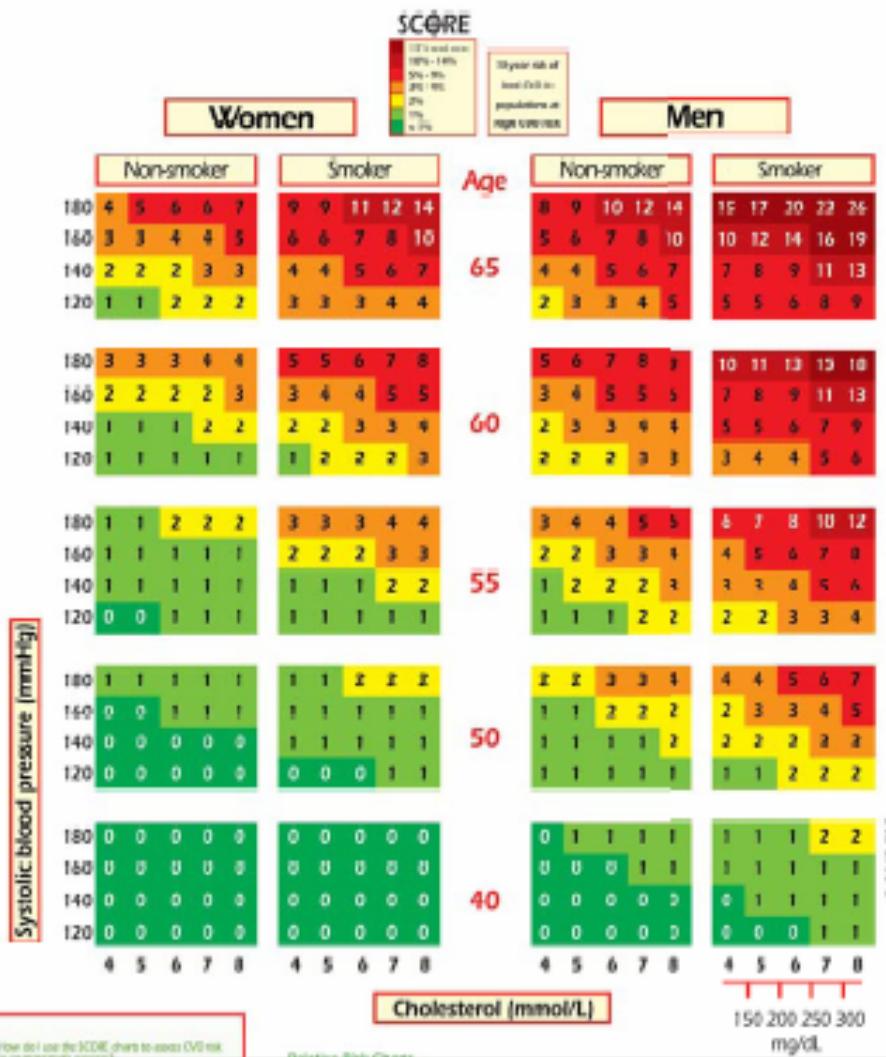


Función endotelial:

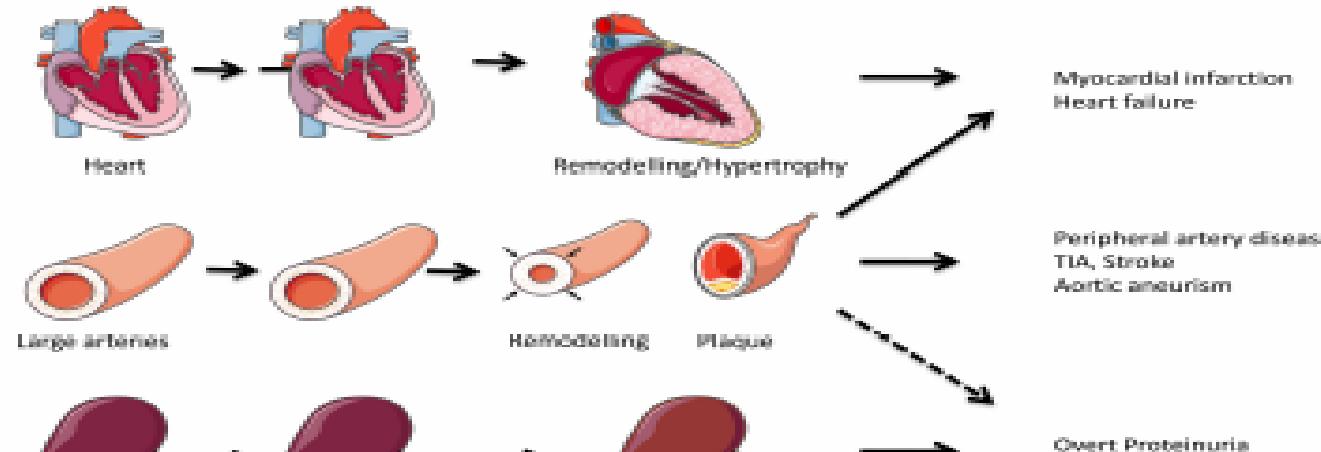
¿a quién?

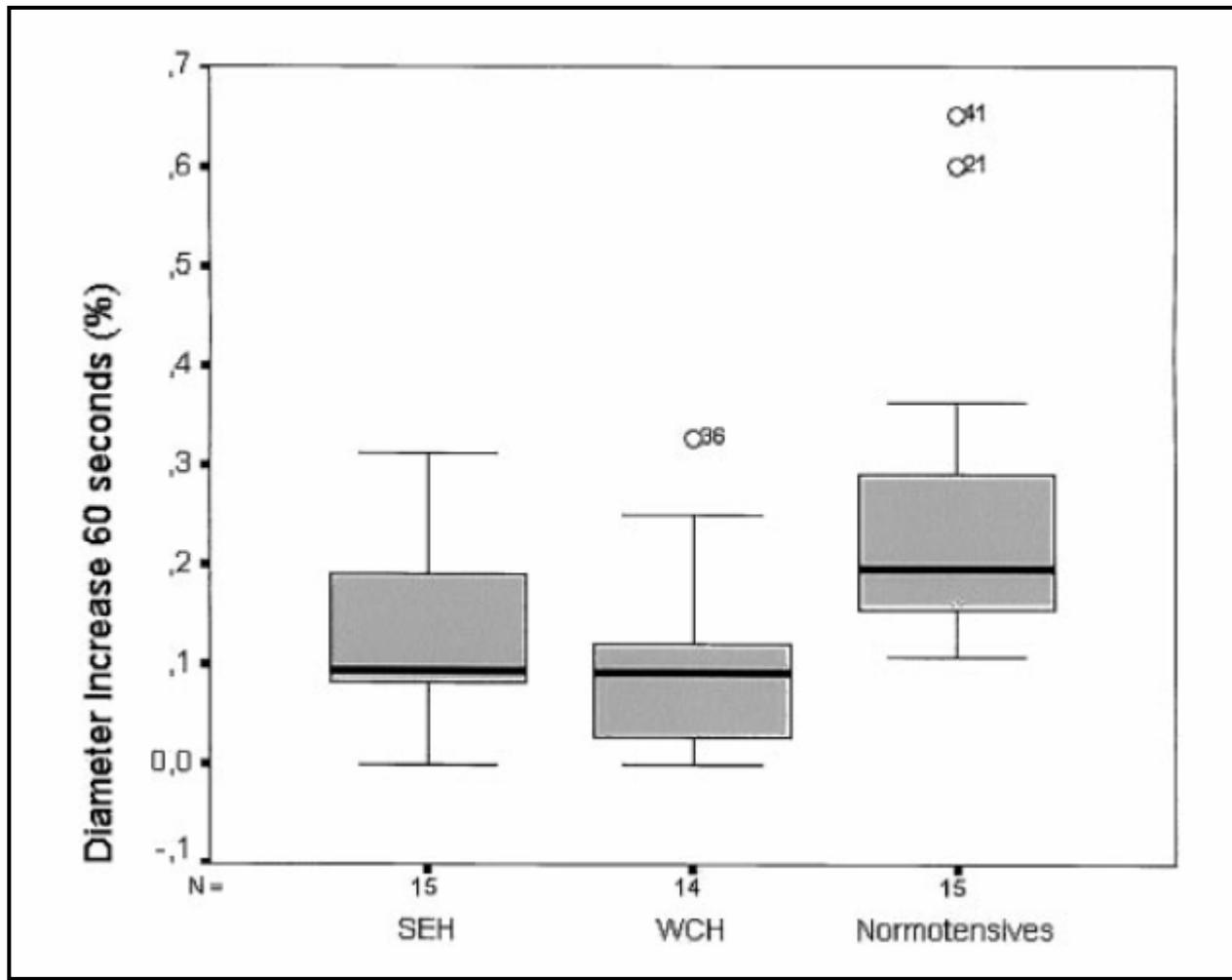
SCORE - European Low Risk Chart

10 year risk of fatal CVD in low risk regions of Europe by gender, age, systolic blood pressure, total cholesterol and smoking status



Endothelial dysfunction and cardiovascular disease





**¿Es la FMD un predictor de
eventos cardiovasculares?**

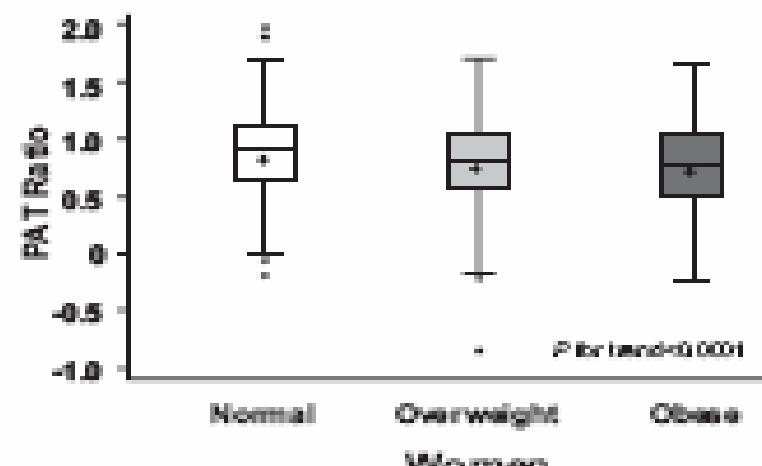
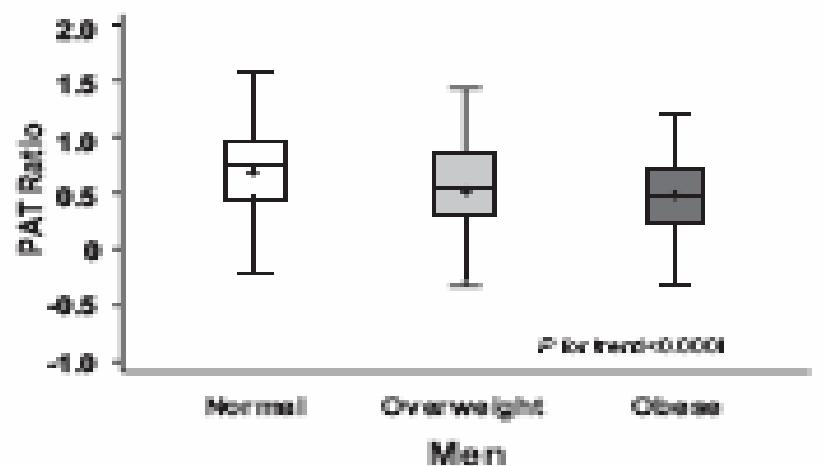
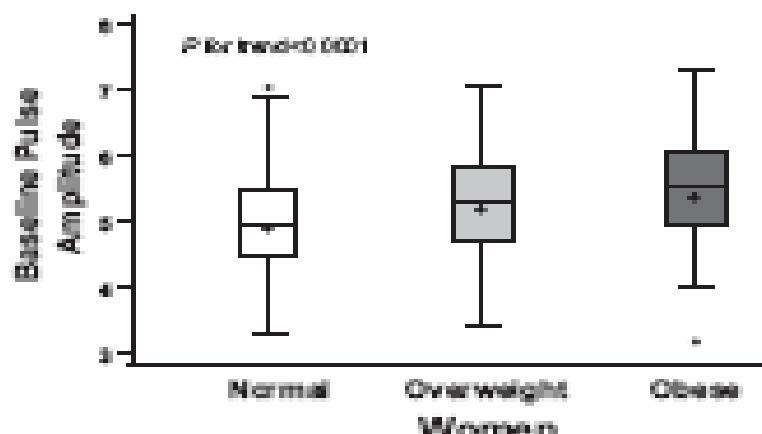
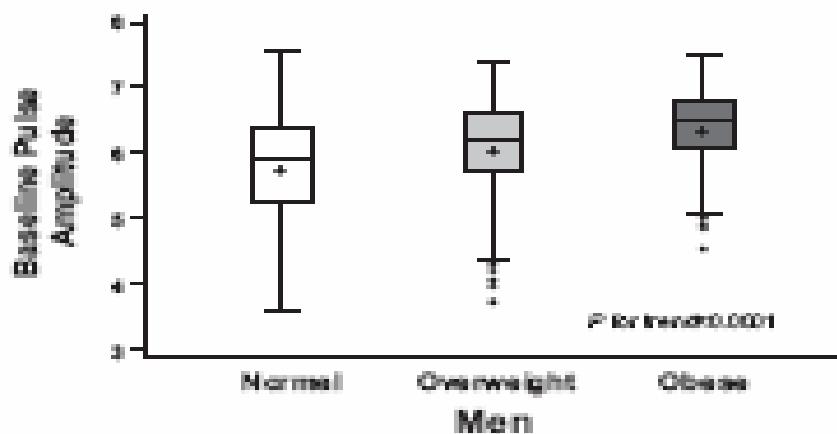


TABLE 2
Studies demonstrating a relationship between endothelial function and prognosis

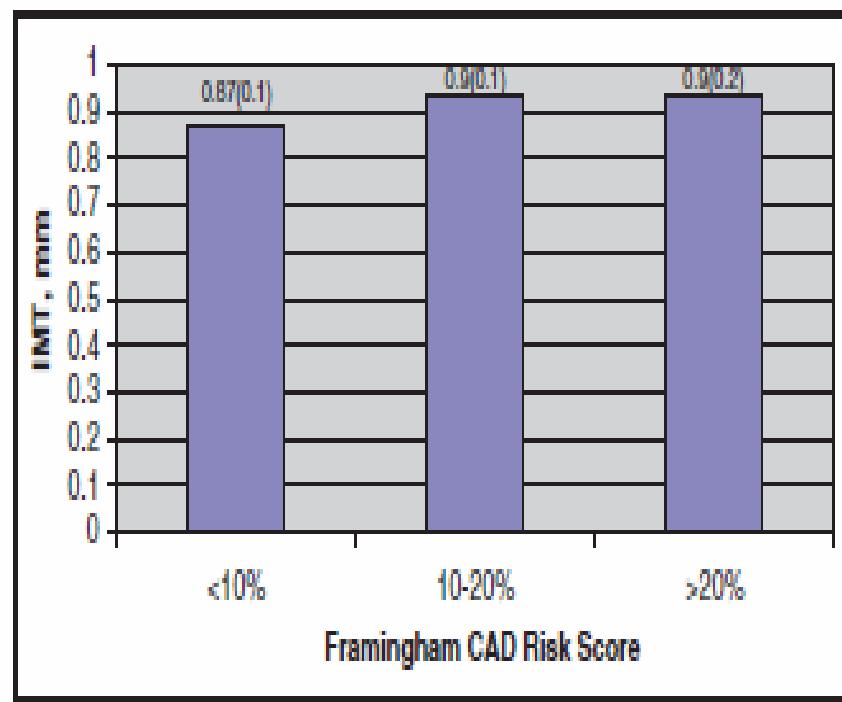
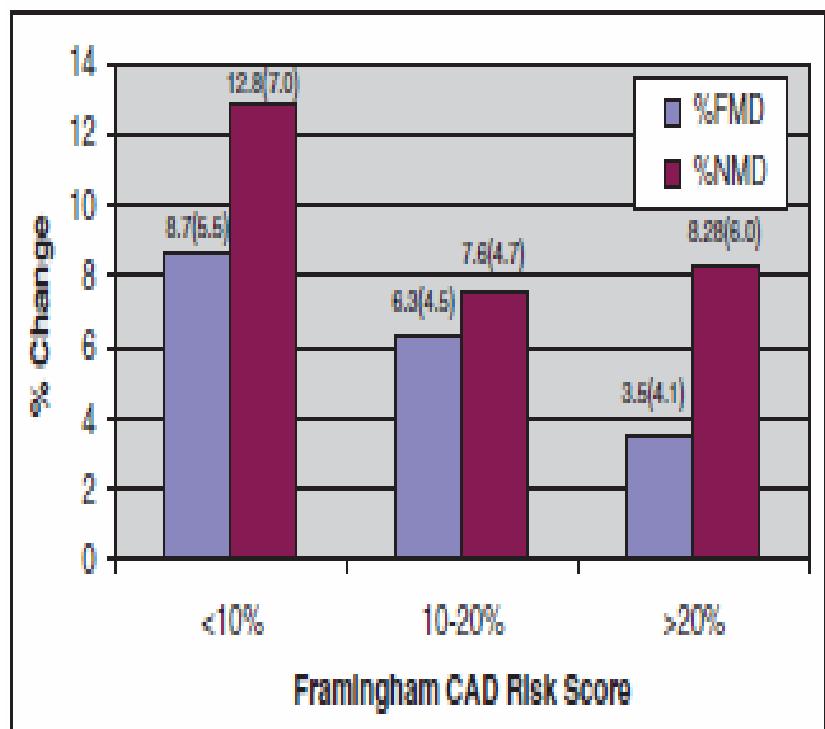
Author	Patient population	Conclusions
Coronary vasomotion		
Al Suwaidi et al (38)	Mild coronary atherosclerosis (n=157)	Predictive of increased rates of myocardial events
Schachinger et al (49)	Chest pain (n=147)	Independently predictive of increased rates of myocardial events
Hollenberg et al (59)	Postcardiac transplant (n=73)	Predictive of CV events
Halcox et al (60)	Patients with and without CAD (n=308)	Independent predictor of CV events
Targonski et al (81)	Patients with mild CAD (n=503)	Independent predictor of cerebrovascular events
Impedance plethysmography		
Perticone et al (14)	Untreated hypertensives (n=225)	Predictive of increased rates of myocardial events in step-wise modelling
Heitzer et al (42)	Patients with CAD (n=281)	Independent predictor of CV events
Fichtlscherer et al (62)	Patients with ACS (n=198)	Response to acetylcholine predictive of events
Flow-mediated dilation		
Modena et al (10)	Post-menopausal female hypertensives (n=400)	Lack of improvement in endothelial dysfunction with antihypertensives associated with CV events
Rossi et al (15)	Postmenopausal women (n=2264)	FMD predictive of CV events beyond traditional risk factors
Yeboah et al (51)	Elderly cohort (n=2792)	FMD predictive of CV events beyond traditional risk factors
Gokce et al (63)	Elective vascular surgery patients (n=187)	FMD independently predictive of CV events
Brevetti et al (64)	Patients with peripheral vascular disease (n=131)	ABI predictive of CV events
Chan et al (65)	Patients in cardiac rehabilitation (n=152)	FMD associated with CV events
Karatzis et al (66)	Patients with NSTEMI (n=98)	FMD independently predictive of CV events
Patti et al (17)	Patients postcoronary stent (n=136)	FMD predictive of restenosis
Shimbo et al (52)	Multiethnic population with varied levels of risk (n=842)	FMD predictive of outcomes, but not in multivariate analysis
Reactive hyperemia		
Huang et al (18)	Vascular surgery patients (n=267)	RH and FMD independently predictive of CV events beyond traditional risk factors

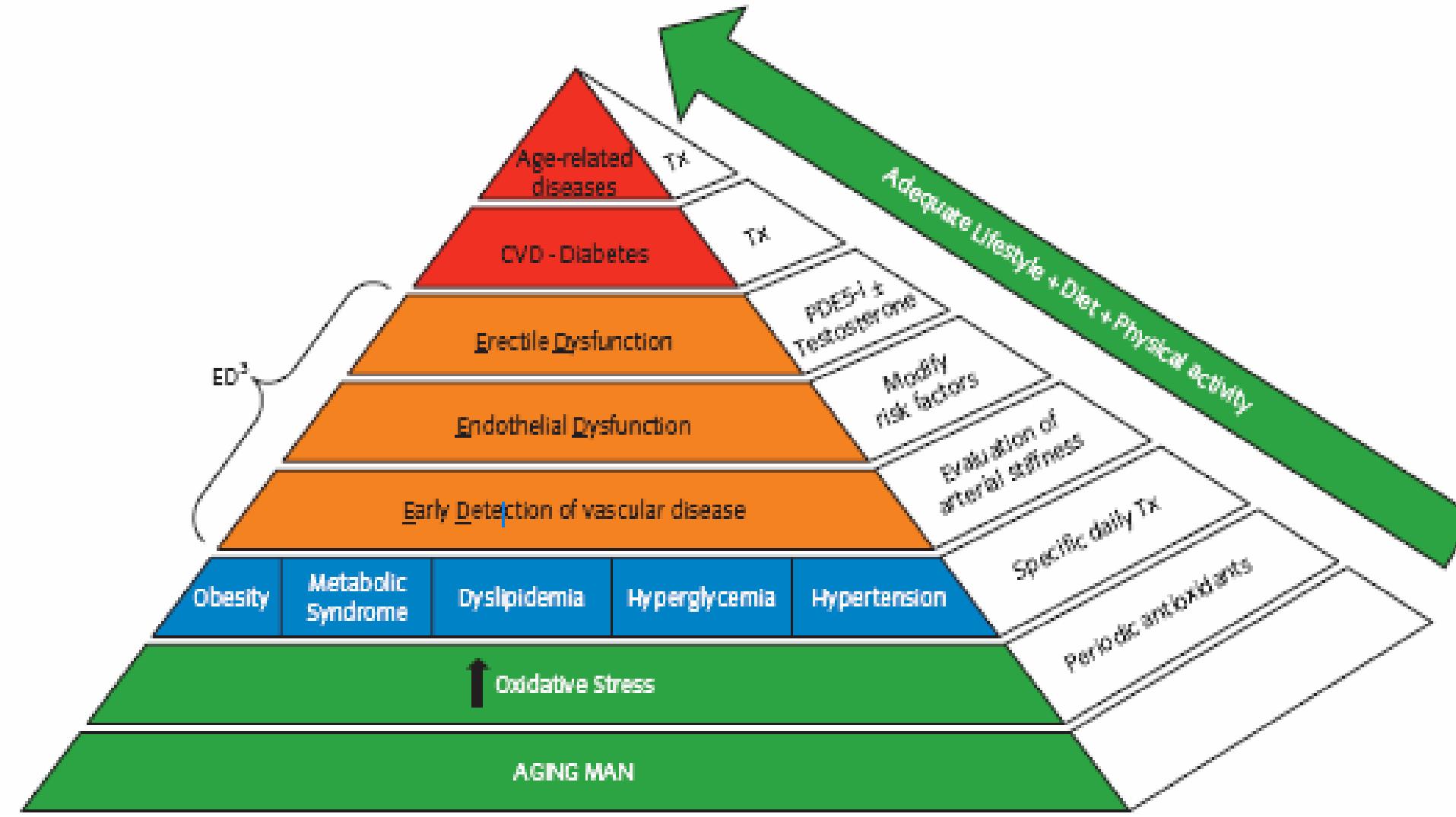
Table adapted from Mancini (58). ABI Ankle-brachial index; ACS Acute coronary syndrome; CAD Coronary artery disease; CV Cardiovascular; FMD Flow-mediated dilation; NSTEMI Non-ST elevation myocardial infarction; RH Reactive hyperemia

Original Paper

The Relationship Between Flow-Mediated Dilatation of the Brachial Artery and Intima-Media Thickness of the Carotid Artery to Framingham Risk Scores in Older African Americans

John Kwagyan, PhD; Saifudin Hussein, MD; Shichen Xu, MD;
Muluemebet Ketete, MD; Abid R. Maqbool, MD; Robert H. Schneider, MD;
Otelio S. Randall, MD





Cross-Sectional Relations of Digital Vascular Function to Cardiovascular Risk Factors in the Framingham Heart Study

- 2008;117:2467-2474.



Assessment of endothelial function by non-invasive peripheral arterial tonometry predicts late cardiovascular adverse events

**Ronen Rubinshtein¹, Jeffrey T. Kuvvin², Morgan Soffler², Ryan J. Lennon³, Shahar Lavi¹,
Rebecca E. Nelson¹, Geralyn M. Pumper¹, Lilach O. Lerman⁴, and Amir Lerman^{1*}**

¹Division of Cardiovascular Diseases, Center of Coronary Physiology and Imaging, Mayo College of Medicine, MB4 523, 200 First Street SW, Rochester, MN 55905, USA; ²Division of Cardiology, Tufts Medical Center, Boston, MA, USA; ³Division of Biomedical Statistics and Informatics, Mayo College of Medicine, Rochester, MN, USA; and ⁴Division of Nephrology and Hypertension, Mayo College of Medicine, Rochester, MN, USA

Received 11 May 2009; revised 2 November 2009; accepted 22 December 2009; online publish-ahead-of-print 24 February 2010

Table 2 Estimated 7 years clinical cardiac adverse event rates in patients undergoing reactive hyperaemia–peripheral arterial tonometry in relation to natural logarithmic scaled reactive hyperaemia index

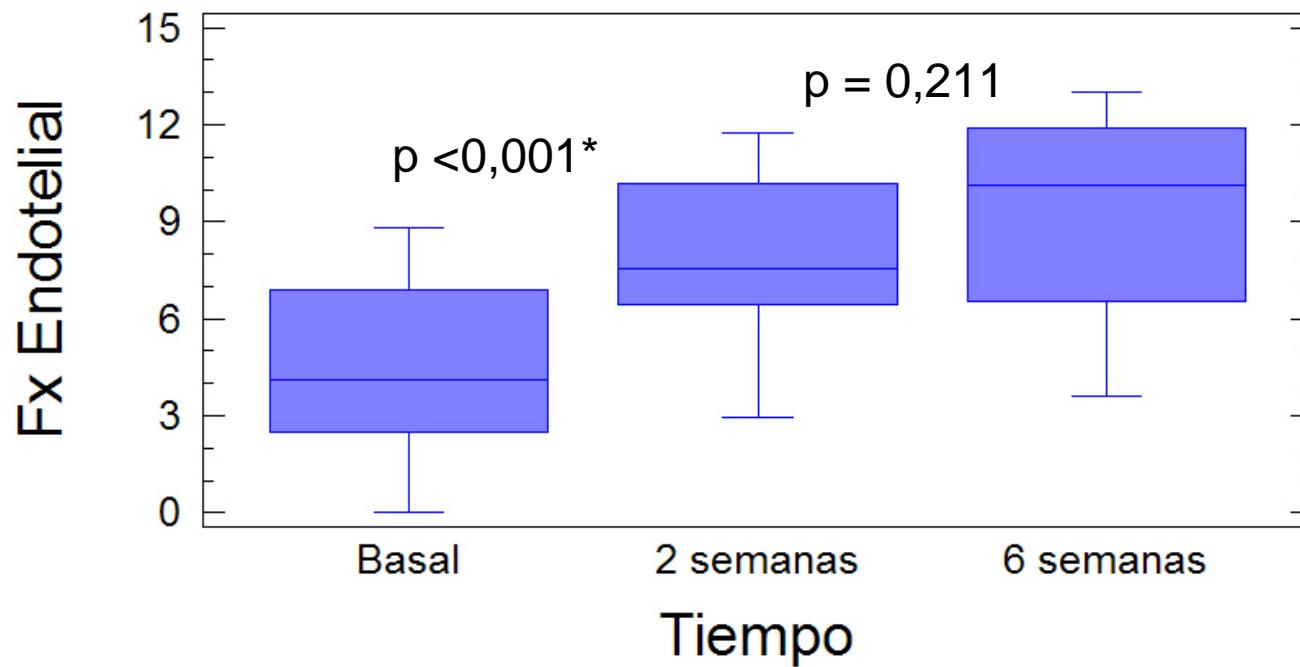
Parameter	Patients with L_RHI < 0.4 (n = 130)	Patients with L_RHI ≥ 0.4 (n = 140)	HR (95% CI)	P-value
CV death	3.9%	0.0%	∞ (1.32, ∞)	0.032
Myocardial infarction	3.4%	3.7%	1.06 (0.27, 4.27)	0.93
Revascularization	12.7%	11.4%	1.21 (0.55, 2.65)	0.64
Stroke	5.3%	3.1%	1.6 (0.45, 5.68)	0.46
CV hospitalizations	30.5%	18.7%	2.06 (1.26, 3.38)	0.018 ^a
AE	48 %	28%	1.83 (1.18, 2.81)	0.030 ^a

^aP-values adjusted for the multiple tests done to identify the optimal cut-point.

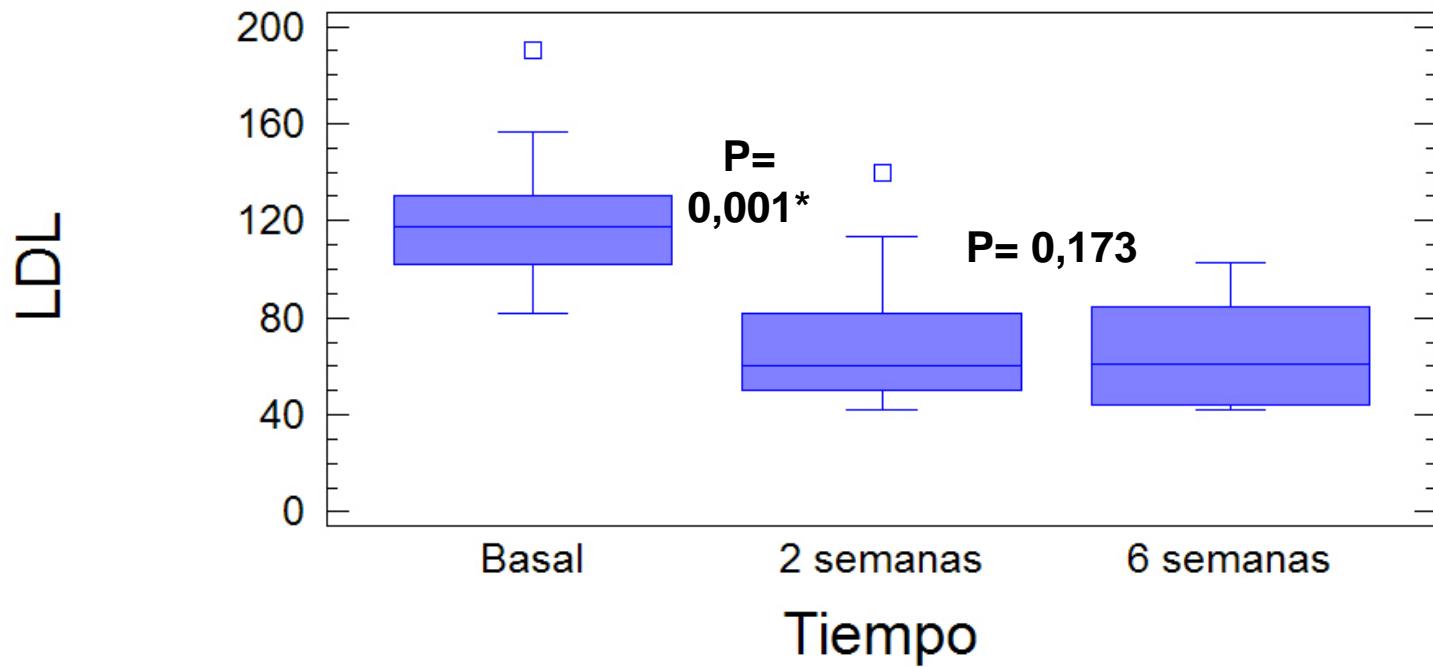
**¿La FMD mejora con el
tratamiento?**

»Sí

Función endotelial

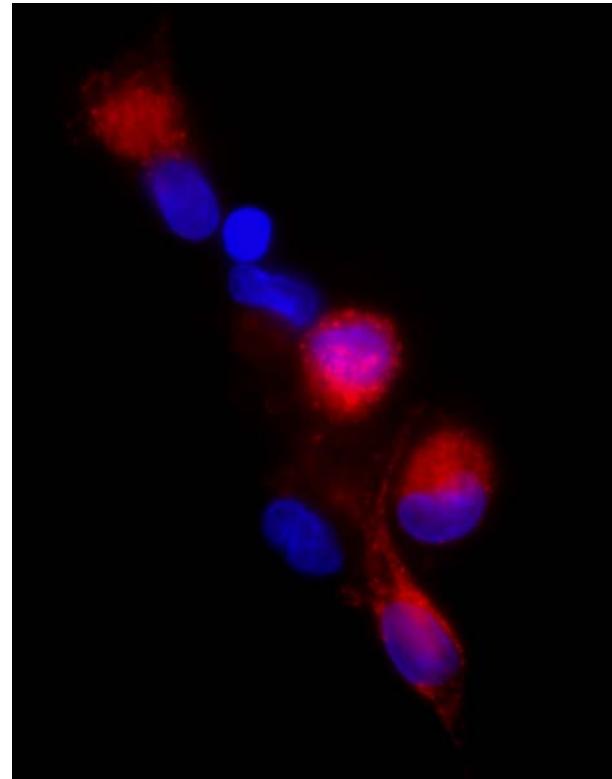
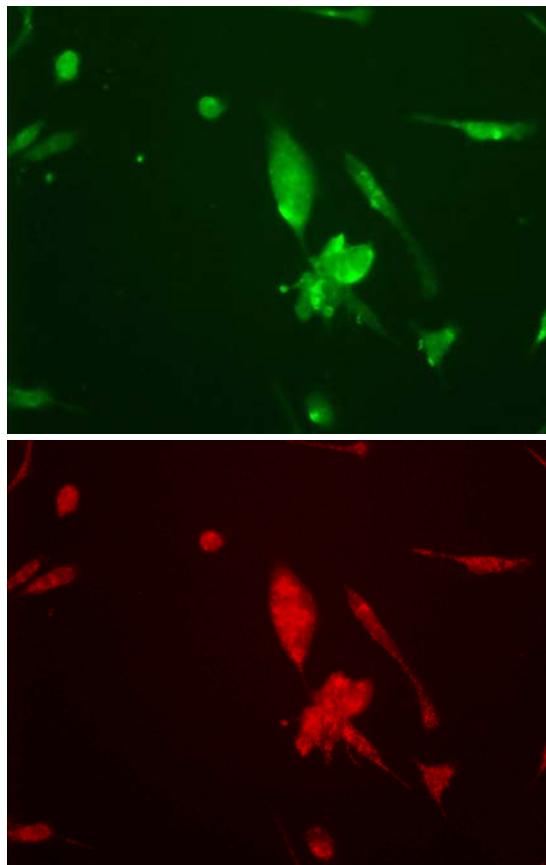


LDL-colesterol



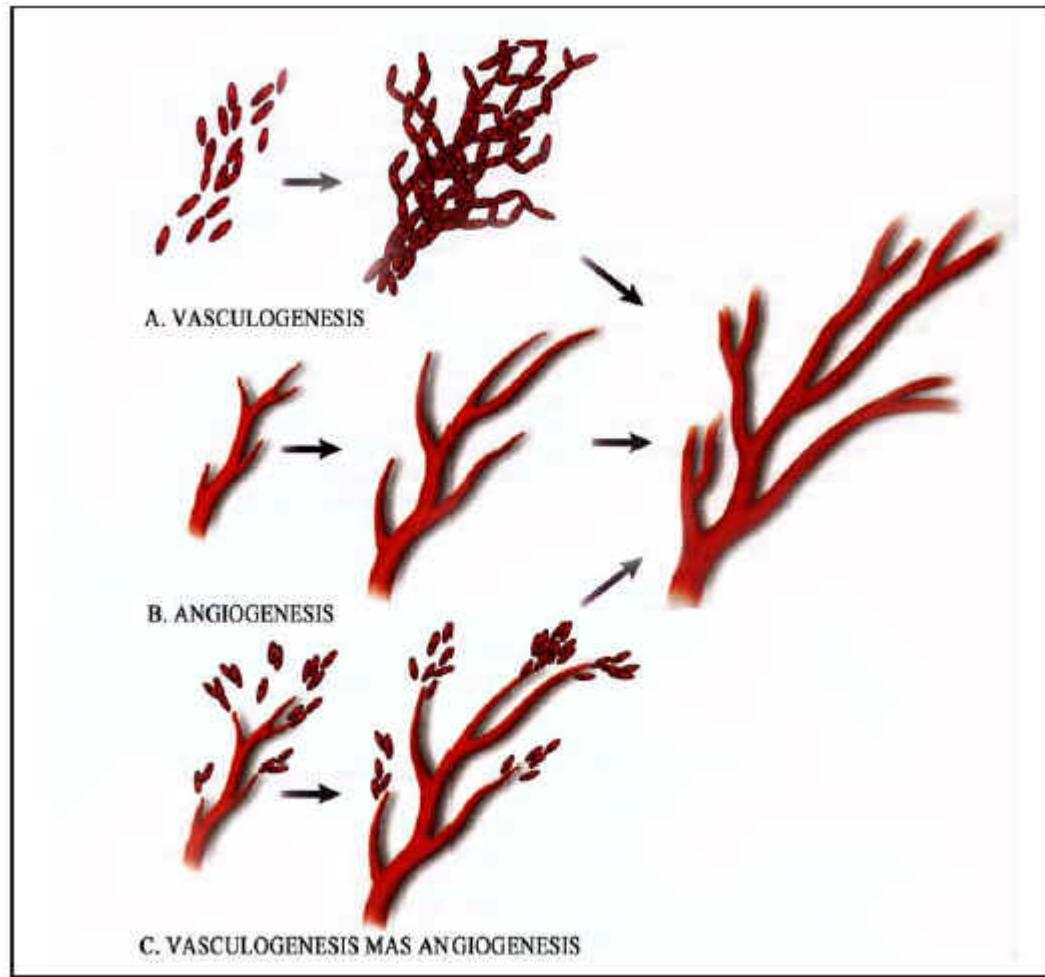
	Basal	2 Semanas	6 Semanas	P
LDL	$119 \pm 26,64$	$71,12 \pm 28,16$	$65,43 \pm 22,17$	< $0,001^*$

Aislamiento CPE: Cultivo

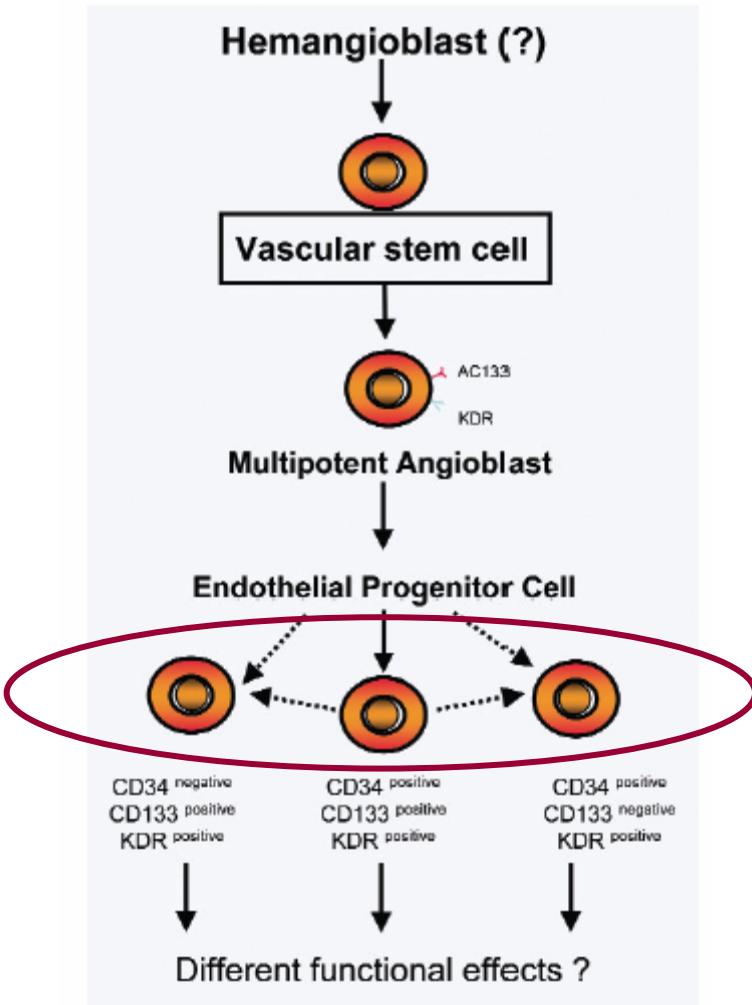


Se utiliza tinción fluorescente para detectar las células que se han marcado con la aglutinina-I del *Ulex europaeus* (UEA-1) y que han incorporado del medio LDL acetiladas, teñidas. Las células con el doble marcaje son consideradas como CPE.

CÉLULAS PROGENITORAS ENDOTELIALES

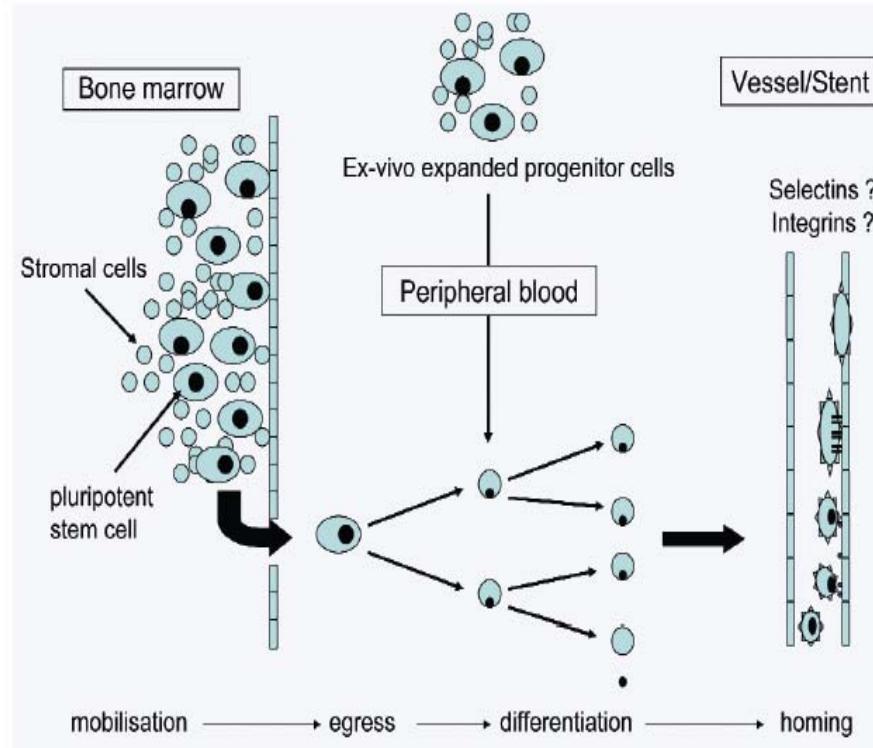


CPE: Biología



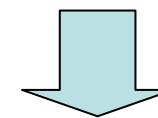
Pool heterogéneo
Distintos estados madurativos

CPE: Función



FUNCIONES

- Re-endotelización**
- Reparación endotelio dañado**



FUNCTION ENDOTELIAL

Factores modificadores CPE

FACTORES ESTIMULANTES DE LAS CPE

Óxido Nítrico

Factor de crecimiento del endotelio vascular (VEGF)

Fármacos:

- o Estrógenos
- o Eritropoyetina
- o Estatinas
- o ARA-II/ IECAs

Eventos isquémicos

FACTORES INHIBIDORES DE LAS CPE

Edad

FRCV

- o HTA
- o DL y LDL
- o DM 1 y 2
- o Tabaco

Homocisteína

CPE

	Basal	2 semanas	6 semanas	P
Cultivo (nº)	$18,88 \pm 31,93$	$27,11 \pm 35,9$	$89,23 \pm 114,55$	$p = 0,02^*$
Citometría (%)	$0,11 \pm 0,09$	$0,048 \pm 0,031$	$0,053 \pm 0,019$	$p = 0,368$

¿Es la resolución de la DE clínicamente relevante ?

1. Antioxidantes
2. Biopterina
3. Reducción peso y sal
4. Ejercicio

- Calcio antagonistas
- B Bloqueantes
- ARA II-IECA-Aliskiren
- Estatinas
- EPO